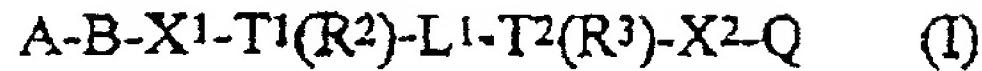


Claims

1. A compound of formula (I)



wherein:

- A is 5- or 6-membered monocyclic aromatic ring containing 1, 2 or 3 ring heteroatoms
 10 selected from nitrogen, oxygen and sulphur atoms optionally substituted by one, two or three atoms or groups selected from halo, oxo, carboxy, trifluoromethyl, cyano, amino, hydroxy, nitro, C₁₋₄alkyl (for example methyl or ethyl), C₁₋₄alkoxy (for example methoxy or ethoxy), C₁₋₄alkoxycarbonyl, C₁₋₄alkylamino (for example methylamino or ethylamino) or di-C₁₋₄alkylamino (for example dimethylamino or diethylamino);
- B is a phenylene ring optionally substituted by one or two substituents selected from halo, trifluoromethyl, trifluoromethoxy, cyano, nitro, C₁₋₄alkyl, C₂₋₄alkenyl and C₂₋₄alkynyl, from the substituent -(CH₂)_nY¹ wherein n is 0-4 and Y¹ is selected from hydroxy, amino, carboxy, C₁₋₄alkoxy, C₂₋₄alkenyloxy, C₂₋₄alkynyloxy, C₁₋₄alkylamino, di-C₁₋₄alkylamino, pyrrolidin-1-yl, piperidino, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, piperazin-1-yl, 4-C₁₋₄alkylpiperazin-1-yl, C₁₋₄alkylthio, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphonyl, C₂₋₄alkanoylamino, benzamido, C₁₋₄alkylsulphonamido and phenylsulphonamido, from the substituent -(CH₂)_nY² wherein n is 0-4 and Y² is selected from carboxy, carbamoyl, C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl, N,N-di-C₁₋₄alkylcarbamoyl, pyrrolidin-1-ylcarbonyl, piperidinocarbonyl, morpholinocarbonyl, thiomorpholinocarbonyl, 1-oxothiomolinocarbonyl, 1,1-dioxothiomolinocarbonyl, piperazin-1-ylcarbonyl, 4-C₁₋₄alkylpiperazin-1-ylcarbonyl, C₁₋₄alkylsulphonamidocarbonyl, phenylsulphonamidocarbonyl and benzylsulphonamidocarbonyl, from a substituent of the formula -X³-L²-Y² wherein X³ is a group of the formula CON(R⁵), CON(L²-Y²), C(R⁵)₂O, O, N(R⁵) or N(L²-Y²), L² is C₁₋₄alkylene, Y² has any of the meanings defined immediately hereinbefore and each R⁵ is independently hydrogen or C₁₋₄alkyl, and from a substituent of the formula -X³-L³-Y¹ wherein X³ is a group of the formula CON(R⁵), CON(L³-Y¹), C(R⁵)₂O,

O, N(R³) or N(L³-Y¹), L³ is C₂₋₄alkylene, Y¹ has any of the meanings defined immediately hereinbefore and each R³ is independently hydrogen or C₁₋₄alkyl, and

wherein any heterocyclic group in a substituent of B optionally bears 1 or 2 substituents selected from carboxy, carbamoyl, C₁₋₄alkyl, C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl and

5 N,N-di-C₁₋₄alkylcarbamoyl, and wherein any phenyl group in a substituent of B optionally bears 1 or 2 substituents selected from halo, trifluoromethyl, cyano, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl,

C₁₋₄alkoxy, C₂₋₄alkenyloxy and C₂₋₄alkynyloxy;

T¹ is CH or N;

10 T² is CH or N;

with the proviso that at least one of T¹ and T² is N and wherein the heterocyclic ring formed by T¹, T², L¹, R² and R³ is optionally substituted by one or two substituents selected from hydroxy, oxo, carboxy and C₁₋₄alkoxycarbonyl; or one of the following:

15 -(CH₂)_n-R, -(CH₂)_n-NRR¹, -CO-R, -CO-NRR¹, -(CH₂)_n-CO-R and -(CH₂)_n-CO-NRR¹;

wherein n is 0, 1 or 2, preferably n is 1 or 2;

R and R¹ are independently selected from hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, hydroxyC₁₋₄alkyl, carboxyC₁₋₄alkyl and C₁₋₄alkoxycarbonylC₁₋₄alkyl or where possible R

20 and R¹ may together form a 5- or 6-membered optionally substituted saturated or partially unsaturated (preferably saturated) heterocyclic ring which may include in addition to the nitrogen to which R and R¹ are attached 1 or 2 additional heteroatoms selected from nitrogen, oxygen and sulphur

X¹ is SO, SO₂, C(R⁴)₂ or CO when T¹ is CH or N; or in addition X¹ is O or S when T¹ is CH;

25 and wherein each R⁴ is independently hydrogen or C₁₋₄alkyl;

L¹ is C₁₋₄alkylene or C₁₋₃alkylenecarbonyl;

R² is hydrogen or C₁₋₄alkyl;

R³ is hydrogen or C₁₋₄alkyl;

or R² and R³ are joined to form a C₁₋₄alkylene or -CH₂CO- group; wherein the ring formed by

30 T¹, R², R³, T² and L¹ is optionally substituted; with the proviso that when T¹ and T² are both N, L¹ is not methylene and R² and R³ together are not methylene;

X² is S(O), wherein y is one or two, C(R⁵), or CO; and each R⁵ is hydrogen or C₁₋₄alkyl; Q is phenyl, naphthyl, phenylC₁₋₄alkyl, phenylC₂₋₄alkenyl, phenylC₂₋₄alkynyl or a heterocyclic moiety containing up to 4 heteroatoms selected from nitrogen, oxygen and sulphur and Q is optionally substituted by one, two or three substituents selected from halo, trifluoromethyl,

- 5 trifluoromethoxy, cyano, hydroxy, amino, nitro, trifluoromethylsulphonyl, carboxy, carbamoyl, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₁₋₄alkoxy, C₂₋₄alkenyloxy, C₁₋₄alkynyloxy, C₁₋₄alkylthio, C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphonyl, C₁₋₄alkylamino, di-C₁₋₄alkylamino, C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl, N,N-di-C₁₋₄alkylcarbamoyl, C₂₋₄alkanoyl, C₂₋₄alkanoylamino, hydroxyC₁₋₄alkyl, C₁₋₄alkoxyC₁₋₄alkyl, carboxyC₁₋₄alkyl, C₁₋₄alkoxycarbonylC₁₋₄alkyl, carbamoylC₁₋₄alkyl, N-C₁₋₄alkylcarbamoylC₁₋₄alkyl, N,N-di-C₁₋₄alkylcarbamoylC₁₋₄alkyl, phenyl, heteroaryl, phenoxy, phenylthio, phenylsulphanyl, phenylsulphonyl, benzyl, benzoyl, heteroaryloxy, heteroarylthio, heteroarylsulphanyl and heteroarylsulphonyl, and wherein said heteroaryl substituent or the heteroaryl group in a heteroaryl-containing substituent is a 5- or 6-membered monocyclic heteroaryl ring containing up to 3 heteroatoms selected from nitrogen, oxygen and sulphur, and wherein said phenyl, heteroaryl, phenoxy, phenylthio, phenylsulphanyl, phenylsulphonyl, heteroaryloxy, heteroarylthio, heteroarylsulphanyl, heteroarylsulphonyl, benzyl or benzoyl substituent optionally bears 1, 2 or 3 substituents selected from halo, trifluoromethyl, cyano, hydroxy, amino, nitro, carboxy, carbamoyl, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylamino, di-C₁₋₄alkylamino,
- 15 20 C₁₋₄alkoxycarbonyl, N-C₁₋₄alkylcarbamoyl, N,N-di-C₁₋₄alkylcarbamoyl and C₂₋₄alkanoylamino;
- and pharmaceutically acceptable salts thereof.

2. A compound of formula (I) according to claim 1 wherein A is a pyridyl, pyrimidinyl or pyridazinyl ring.

3. A compound of formula (I) according to claim 2 wherein A is 4-pyrimidinyl or 4-pyridyl.

30 4. A compound of formula (I) according to any one of claims 1 to 3 wherein B is paraphenylene.

5. A compound of formula (I) according to any one of claims 1 to 4 wherein the ring formed by T¹, R², R³, T² and L is 1,4-piperazinediyl.
- 5 6. A compound of formula (I) according to any one of claims 1 to 5 wherein X¹ is CO.
7. A compound of formula (I) according to any one of claims 1 to 6 wherein X² is SO₂.
8. A compound of formula (I), as defined in claim 1, wherein
10 A is pyridyl, pyrimidinyl, or pyridazinyl;
B is para-phenylene;
X¹ is CO, SO₂ or CH₂;
T¹ and T² are both N;
L¹ is ethylene or propylene;
15 R² and R³ are joined to form an ethylene or propylene or methylenecarbonyl group;
X² is SO₂;
Q is styryl or naphthyl optionally substituted by fluoro, chloro or bromo or is phenyl
optionally substituted by fluorophenyl, chlorophenyl, or bromophenyl;
and pharmaceutically-acceptable salts thereof.
20
9. A compound of formula (I) selected from:
1-(6-bromonaphth-2-ylsulphonyl)-4-[4-(4-pyrimidinyl)benzoyl]piperazine;
1-(6-chloronaphth-2-ylsulphonyl)-4-[4-(4-pyridyl)benzoyl]piperazine;
1-(6-bromonaphth-2-ylsulphonyl)-4-[4-(4-pyridazinyl)benzoyl]piperazine;
25 and pharmaceutically-acceptable salts thereof.
10. A compound of formula (I) according to any one of claims 1 to 9 for use in medical therapy.
- 30 11. A pharmaceutical formulation comprising a compound of formula (I) according to any one of claims 1 to 9 and a pharmaceutically-acceptable diluent or carrier.

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12. Use of a compound of formula (I) according to any one of claims 1 to 9 in the preparation of a medicament for use in producing a Factor Xa inhibiting effect.

5 13. A method of preventing or treating a Factor Xa mediated disease or medical condition comprising administering to a patient a pharmaceutically effective amount of a compound of formula (I), as defined in any one of claims 1 to 9.

14. A process for preparing a compound of formula (I), as defined in claim 1,
10 comprising:

(a) for the production of those compounds of the formula (I) wherein T¹ is N and X¹ is CO, the reaction, conveniently in the presence of a suitable base, of an amine of formula (II)

$$15 \quad HN(R^2) - L^1 - T^2(R^3) - X^2 - Q \quad (II)'$$

with an acid of the formula (III)

$$A \cdot B \cdot COOH \quad (III)$$

20 or a reactive derivative thereof;

(b) for the production of those compounds of the formula (I) wherein T¹ is CH and X¹ is O by the reaction, conveniently in the presence of a suitable coupling agent, of a compound of the formula (IV):

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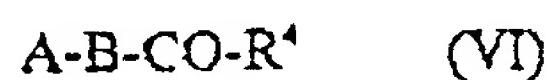
$$Z-CH(R^2)-L^1-T^2(R^3)-X^2-Q \quad (IV)$$

wherein Z is a displaceable group, with a phenolic compound of the formula (V):

30 A-B-OH (V):

- 48 -

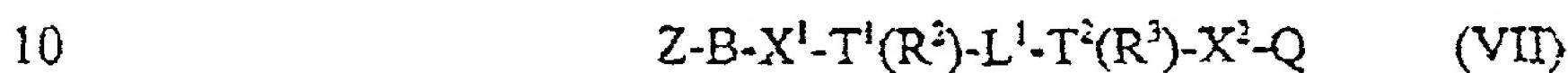
- (c) for the production of those compounds of the formula (I) wherein T¹ is N and X¹ is CH(R⁴), the reductive amination of a keto compound of the formula (VI):



5

wherein R⁴ is hydrogen or C₁₋₄ alkyl, with an amine of the formula (II) as defined above;

- (d) the reaction of a compound of the formula (VII):

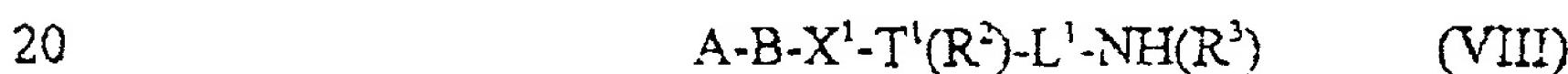


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wherein Z is a displaceable group with an activated derivative of ring A;

- (e) by forming A ring on compounds of formula (VII), wherein Z is a functional group capable of cyclisation;

- (f) for the production of compounds wherein T² is N, the reaction of a compound of the formula (VIII):



with a compound of the formula (IX):

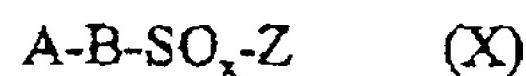


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wherein Z is a displaceable group;

- (g) for the production of compounds wherein T¹ is N and X¹ is SO or SO₂, the reaction of a compound of the formula (II) as defined above with a compound of the formula (X):

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wherein x is one or two and Z is a displaceable group;

- (h) for production of compounds of formula (I) by coupling T² to Q and thus preparing
5 the -T²-X²-Q moiety, methods analogous to those described in process variants (a), (c) and (g)
for preparing the B-X¹-T¹- moiety may be employed;
- (i) for the production of compounds of formula (I) wherein X¹ is a group of the
formula SO, SO₂, wherein B bears a C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphonyl,
10 1-oxothiomorpholino or 1,1-dioxothiomorpholino group, wherein X² is a group of the formula
SO or SO₂ wherein Q bears a C₁₋₄alkylsulphanyl, C₁₋₄alkylsulphonyl, phenylsulphanyl,
phenylsulphonyl, heteroarylsulphanyl or heteroarylsulphonyl group, the oxidation of the
corresponding compound of the formula (I) which contains X¹ as a thio group.